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VASCULAR DISEASE

EFFECTS OF TELMISARTAN AND RESVERATROL ON MONOCYTE ADHESION TO THE ENDOTHELIUM EXPOSED TO DISTURBED FLOW AND INFLAMMATION

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Background: Atherosclerotic plaques develop at arterial regions subjected to disturbed flow ('non-uniform shear stress'), and are initiated by increased leukocyte-endothelial interactions. Here we applied the in vitro model of arterial bifurcations to investigate whether anti-inflammatory compounds such as the angiotensin II type 1 receptor blocker telmisartan, or resveratrol, an anti-inflammatory plant polyphenol from red wine, prevent monocyte recruitment by endothelium.

Methods: Human umbilical vein endothelial cells (ECs) were exposed to laminar or non-uniform shear stress in bifurcating flow-through slides, followed by 2h stimulation with 2.5 ng/mL TNF-a. During flow, cells were incubated either with telmisartan or with resveratrol. To study cell adhesion, ECs were perfused with medium containing THP-1 monocytic cells. Adherent THP-1 monocytes were quantified by light microscopy. Endothelial protein expression was determined by immunofluorescence.

Results: We observed a dramatic increase in monocytic cell adhesion to endothelial cells exposed to non-uniform shear stress at bifurcations in combination with TNF-a. This induction of monocytic cell recruitment was accompanied by a significant increase in the expression of E-selectin and vascular cell adhesion molecule (VCAM)-1. In cells treated with telmisartan (1-20 µmol/L) during exposure to shear stress, progressive inhibition of monocytic cell adhesion was observed, with about 45% reduction at 1 µmol/L. This effect was mediated by a significant reduction of endothelial VCAM-1 expression. On the contrary, E-selectin expression was not affected by telmisartan. Resveratrol (10-100 µmol/L) dose-dependently inhibited the expression of both VCAM-1 and E-selectin, and reduced monocytic cell recruitment by 50% at 20 µmol/L.

Conclusions: Pharmacological treatment with telmisartan and resveratrol decreases the TNF-a-induced recruitment of monocytic cells and the endothelial expression of adhesion molecules in regions of non-uniform shear stress in vitro. This mechanism can contribute to the beneficial pleiotropic effects of either telmisartan or resveratrol in atherosclerosis-prone arterial regions in vivo.